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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/462,816	04/05/2000	XIAOMAO LI	1038-1003-M1	5549

7590

06/27/2003

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EXAMINER

WHITEMAN, BRIAN A

ART UNIT	PAPER NUMBER
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1635

22

DATE MAILED: 06/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/462,816

Applicant(s)

LI ET AL.

Examiner

Brian Whiteman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 April 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9,13-23,27,28,30-34,39,49 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9,13-23,27,28,30-34,39,49 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 05 April 2000 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 21.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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DETAILED ACTION

Non-Final Rejection

Claims 1-9, 13-23, 27, 28, 30-34, 39, and 49 are pending.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/8/03 has been entered.

The applicants' traversal, the amendment to claims 15, 30, and 49 in paper no. 20 filed on 4/8/03 is acknowledged and considered.

In paper no. 20, filed on 4/8/03, the status of claim 41 is pending. However, claims 40-42 were cancelled in paper no. 15 filed on 10/10/02. Clarification for the status of this claim is requested.

Drawings

New corrected drawings are required in this application because of the objection by the draftsman, see paper no. 7 filed on 5/22/01. Applicant is advised to employ the services of a competent patent draftsman outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action

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to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Claim Objections

Claims 1, 15, and 30 are objected to because of the following informalities: nucleotide sequences do not “encode” introns although they may comprise an intron. Appropriate correction is required.

Claim Rejections - 35 USC § 112

Applicant's arguments, see paper no. 20, filed on 4/8/03, with respect to 112 first paragraph enablement have been fully considered and are persuasive. The rejection of claims 1-9, 13-23, 27-34, and 39-42 has been withdrawn because of the amendment to claim 15 and the cancellation of claims 40 and 42.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-9, 13-23, 27, 28, 30-34, 39, and 49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-9, 13-23, 27, 28, 30-34, 39, and 49 are indefinite because the claims require a “plasmid that will not replicate” and there is no such plasmid. A plasmid by definition, must replicate autonomously in an appropriate cell (See Lodish et al., Molecular Cell Biology, Fourth Edition, WH FREEMAN, New York, New York, 2000, Glossary, term: plasmid.).

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Applicant's arguments with respect to claims 1-9, 13-23, 27, 28, 30-34, 39, and 49 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a), which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or non-obviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2, 5-7, 15-16, 19-20, 30-34, and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Olmsted et al. (1989, J. Virol., Vol. 63 (1), 411-420) and Simard et al. (Antiviral Research, Vol. 28, pp. 303-315, 1995) in view of Johnson et al. (1987, Proc. Natl. Acad. Sci., Vol. 84, 5625-5629), Wagener et al. (1996, J. Biotech., Vol. 44, 59-65), Norman et al. (June, 1997, Vol. 15 (8), 801-803), and Haddad et al. (July, 1997, Vol. 18, 193-202). Olmsted teaches recombinant vaccinia viruses, which encode either full length or truncated versions of the human RSV G protein, and demonstrates that intranasal administration to rats with the recombinant G protein encoding vaccinia viruses resulted in significant anti-RSV G protein antibody titers (Olmsted et al., page 412, Figure 1, and page 417, Table 1). Olmsted et al. further teaches that the G protein from three strains of RSV, including the Long strain has been sequenced (Olmsted et al., page 411, column 2). Simard also teaches recombinant vaccinia viruses comprising an RSV G protein. Specifically, Simard teaches a fragment corresponding to amino acids 124-203 of the RSV G protein of the Long strain which lacks the trans-membrane region and sequences upstream (Simard et al., page 311, paragraph 2). Simard et al. also teaches that administration to mice with the recombinant plasmid generated significant anti-RSV antibody titers (Simard et al., page 310, Table 1). It is further noted that Simard comments that the vaccinia virus is not expected to become a suitable vector for the development of human vaccines (Simard et al., page 313, paragraph 2). Johnson supplements both Olmsted, and Simard by providing the amino acid sequence of the G protein derived from the Long strain of RSV which is 99.1% identical to the nucleic acid sequence encoding applicants SEQ ID NO: 2 (Johnson et al., page 5627, Figure 2). However, Olmsted and Simard differ from the instant invention in that they utilize replicating vectors i.e. vaccinia virus.

However, at the time the invention was made, Simard suggests that the vaccinia virus is not the vector of choice for use in humans. Wagener supplements Olmsted and Simard by teaching that immunogenic compositions may be safer than live attenuated viruses and that immunogenic compositions comprising a plasmid can be used to induce an immune response similar in scope to attenuated viruses (Wagener et al., page 60, paragraph 2). More specifically, Wagener teaches that administration to mice with a non-replicating plasmid vector encoding a CMV promoter and comprises a CMV intron A operatively linked to the tissue plasminogen activator (tPA) leader sequence and the SIV gp130 antigen resulted in significant titers of anti-SIV antibodies (Wagener et al., pages 62- 63, and Figures 2+ 3). Norman supports Wagener by teaching that the optimized plasmid vector for gene expression and delivery *in vivo* includes a CMV promoter and enhancer and the CMV IE intron A (Norman et al., page 801, abstract). Haddad further supports Wagener by teaching that the addition of the tPA signal sequence is warranted in order to prevent retention of peptides in the cytoplasm and to ensure proper glycosylation in the ER (Haddad et al., page 201, paragraph, 3).

Therefore, in view of the optimal nature of the plasmid vector taught by Wagener et al. which includes the CMV promoter, CMV intron A, and the tPA signal sequence as taught by Norman and Haddad, and in view of the teachings of Wagener which support the use of plasmid vector over attenuated viral vectors to induce antigen specific antibodies, it would have been *prima facie* obvious to the skilled artisan to use the plasmid vector taught by Wagener to express the RSV G proteins taught by Olmsted, Johnson, or Simard in order to generate anti-RSV antibody responses *in vivo*. Further based on the well known techniques of molecular biology and the teachings of Olmsted and Simard that the RSV G protein are produced *in vivo*, the skilled

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artisan would have had a reasonable expectation of success in making a plasmid encoding CMV promoter and comprising a CMV intron A, and the tPA signal sequence and encoding an RSV G protein and using said plasmid to produce an immunogenic composition used to produce antibodies that specifically react with RSV G protein in a mammal.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicant's arguments filed on 4/8/03 have been fully considered but they are not persuasive for the reasons set forth above.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the administration of the plasmid to a host produces a balanced Th1/Th2 cytokine profile) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Claims 1-2, 5-7, 15-16, 19-20, 30-34, and 49 are rejected under 35 U.S.C. 103(a) as being Stott et al. (Journal of Virology, Vol. 60, pp. 607-613, 1986) and Johnson et al. (1987, Proc. Natl. Acad. Sci., Vol. 84, 5625-5629) taken with Simard et al. (Antiviral Research, Vol. 28, pp. 303-315, 1995), Wagener et al. (1996, J. Biotech., Vol. 44, 59-65) and Haddad et al. (July, 1997, Vol. 18, 193-202) in further view of Herrmann et al. (Applicants' IDS, US patent 5,620,896, 1997).

Stott teaches that RSV G protein expressed from a recombinant vector can produced antibodies specific for the RSV G protein (abstract). Stott produced a plasmid containing a complete cDNA copy of the RSV G gene (page 607). Stott further teaches that the G protein expressed from the recombinant vector induced antibodies in rabbits (page 607). Johnson supplements Stott by providing the amino acid sequence of the RSV G protein derived from the Long strain of RSV which is 99.1% identical to the nucleic acid sequence encoding applicants SEQ ID NO: 2 (Johnson et al., page 5627, Figure 2). However, Stott and Johnson differ from the instant invention that Stott utilized a vaccinia virus vector.

However, at the time the invention was made, Simard suggests that the vaccinia virus is not the vector of choice for use in humans. Wagener supplements Simard by teaching that immunogenic compositions may be safer than live attenuated virus vaccines and that immunogenic compositions induce immune responses similar in scope to attenuated viruses (Wagener et al., page 60, paragraph 2). More specifically, Wagener teaches that administration to mice with a non-replicating plasmid vector encoding a CMV promoter and comprises a CMV intron A operatively linked to the tissue plasminogen activator (tPA) leader sequence and the SIV gp130 antigen resulted in significant titers of anti-SIV antibodies (Wagener et al., pages 62-63, and Figures 2+ 3). Haddad further supports Wagener by teaching that the addition of the tPA signal sequence is warranted in order to prevent retention of peptides in the cytoplasm and to ensure proper glycosylation in the ER (Haddad et al., page 201, paragraph, 3). Furthermore, Herrmann provides a control plasmid pCMVIA, a bacterial plasmid that includes SV40 replication origin, the CMV promoter, Intron A and a bovine growth hormone gene that provides a polyadenylation signal (column 5, lines 56-63). Furthermore, Herrmann uses the plasmid,

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wherein the promoter is operably linked to a nucleotide sequence encoding a rotavirus polypeptide wherein said rotavirus polypeptide is expressed in a cell of a mammal with said plasmid vector (column 27, lines 39-45).

It would have been *prima facie* obvious for a person of ordinary skill in the art at the time the invention was made to modify the teaching of Stott and Johnson taken with Simard, Wagener, and Haddad in further view of Herrmann to produce an immunogenic composition comprising a RSV G protein to produce an immune response in a mammal. One of ordinary skill in the art would have been motivated to produce this composition since it would facilitate the expression of antibodies specific for the RSV G protein when administered to a mammal.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicant's arguments with respect to claims 1-2, 5-7, 15-16, 19-20, and 30-34 have been considered but are moot in view of the new ground(s) of rejection.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 15, 16, 17, 18, 19, 20, 21, 22, 23, 30-34, 39 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 30, 31, 32, 33, 34, 35, 36, 37, 38, and 39 of co-pending Application No. 09/272,262. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications are directed to a method of stimulating an immune response in a mammal comprising using an immunogenic composition comprising a plasmid that will not replicate, wherein the plasmid comprises: a first nucleotide sequence encoding a RSV G protein; a promoter sequence operatively linked to said first nucleotide sequence and a second nucleotide sequence encoding the human CMV intron A located between said first nucleotide sequence and said promoter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant's arguments with respect to claims 15, 16, 17, 18, 19, 20, 21, 22, 23, 30, 39 have been considered but are moot in view of the new ground(s) of rejection.

Claims 1, 2, 3, 4, 5, 6, 7, 8, 9, 13-23 and 27 and 28 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 6, 7, 10, 11, 13 and 14 of co-pending Application No. 08/896,442. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications are directed to making and using an immunogenic composition comprising a plasmid that will not replicate, wherein the plasmid comprises: a first nucleotide sequence

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encoding a RSV G protein; a promoter sequence operatively linked to said first nucleotide sequence and a second nucleotide sequence encoding the human CMV intron A located between said first nucleotide sequence and said promoter. In addition, both applications are directed to a plasmid vector PXL5 or PXL6.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant's arguments with respect to claims 1, 2, 3, 4, 5, 6, 7, 8, 9, 13-23, and 27 and 28 have been considered but are moot in view of the new ground(s) of rejection.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (703) 305-0775. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader, SPE - Art Unit 1635, can be reached at (703) 308-0447.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

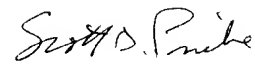
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Brian Whiteman

Patent Examiner, Group 1635



SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER